DRAFT #4 SOH comment on "local context"

The phrase "local context" does not appear in the federal regulations (45CFR46 or 21CFR56). The concept of "local context" was birthed in guidance. In 1998 the Office for Protection from Research Risks (OPRR - now the Office for Human Research Protection - OHRP) issued internal guidance for OPRR staff on "local context," which stated: "Institutions have a profound responsibility to ensure that all IRBs designated under an OPRR-approved Assurance possess sufficient knowledge of the local research context to satisfy these requirements [45 CFR 46.103(d), 45 CFR 46.107(a)(i-ii), 45 CFR 46.111(a)(3),(a)(4),(a)(7),(b), and 46.116]. This responsibility endures regardless of the IRB's geographic location relative to the institution and the research. It is particularly critical where the research involves greater than minimal risk to subjects or vulnerable categories of subjects." This guidance was updated in 2000 and stands today as current OHRP guidance.

Because of the "local context" guidance, institutions are reluctant to cede authority for IRB review and central IRBs have had to develop burdensome procedures – to the IRBs and to investigators and institutions – for site demographic data and communication, which offer little enhancement to human subject protection.

The 1998 staff memo was written at a time when several universities were turning to independent review boards as a result of adverse actions (e.g., suspension of assurance of compliance) taken by OPRR against these institutions. At that time, there was wide perception by the research community that OPRR did not favor central review, especially if the review was conducted by an independent review board (i.e., "commercial" and/or not institutionally affiliated). This perception was partially tied to the fact that federal assurances were only issued to "institutions," so "independent IRBs" were not eligible for an assurance. This view about the use of independent review boards has changed in recent years at OHRP.

In a correspondence letter dated April 13, 2010, the current Director of OHRP stated: "OHRP is taking steps to address institutions' concerns about relying on an IRB external to the institution. For example, … we have archived prior guidance documents ["Local IRB Review of Multicenter Clinical Trials" [1992] and "Local Institutional Review Board (IRB) Review of Multicenter Clinical Trials Sponsored by the Division of Aids (DAIDS) National institute of Allergy and Infectious Diseases (NIAID)" [1993]] that suggested OHRP favors local IRB review over review by a non-local IRB, a position that OHRP no longer holds. (The reviewing IRB should nonetheless have appropriate knowledge of the local context.)"

Whereas the guidance offered in this response letter supports IRB review by a non-local IRB, it still reinforces the requirement that the reviewing IRB must have special knowledge about the local context and further that the concept of "local context" is essential to the regulatory compliance of the IRB in reviewing research.

FDA has historically supported central review and review by independent review boards. However, in the 2006 FDA guidance (Using a Centralized IRB Review Process in Multicenter Clinical Trials), it states that, "An IRB that is at a different location from the research site can review the research, provided that the IRB is competent to understand the local context of the

research. As stated in 21 CFR 56.107(a), this would require sensitivity to community attitudes and the ability to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice."

Again, while the FDA appears to allow IRBs to have employ a less stringent standard in meeting the requirement for local context (confining it to the IRB membership requirements found in section 56.107), there is still appears to be a new (as of 2006) absolute requirement that the IRB be composed to understand the local context at all sites in which the research would be conducted.

Clearly, both the OHRP and FDA guidance documents are outdated. Many publicly and most privately funded research studies involve multiple sites and support a single IRB that has primary responsibility for review and approval of the research (e.g., an independent review board for industry-sponsored clinical trials, NCI central IRB for NCI-funded trials, or the Partners Healthcare System serving as a central IRB for NINDS-funded research). Because research design and methods must be standardized across sites, and the only flexibility within the protocol is to minimally tailor the consent document, local context takes on less importance in protecting human subjects. IRBs that conduct review for multiple sites collect information about the local setting – local resources, including staffing available to conduct the research, demographic information about the study population, and the consent process – to fulfill the requirement to consider local context. However, the burden of collecting this information might not be justified based on its limited use in protecting research subjects.

Further, even without the recent changes in the research enterprise to more multi-site and collaborative research, the notion that any IRB always has sufficient competence to judge the local context is naïve. In large urban areas where there are hundreds of ethnic groups and languages spoken, an IRB, no matter whether it is located within an institution or is centrally located, will not have the competence to judge local context beyond what is acceptable practice by central or independent review boards.

SOH/SACHRP recommends that OHRP and FDA retire their respective guidance documents and issue guidance, which encourages single IRB review under a "reliance model" that allows an institution to use an external IRB (whether central or independent or other type of single IRB review model) that is deemed competent if its policies and procedures comply with the federal regulations related to IRB composition and review procedures. The use of the term "local context" should be expunged.